

## **REMARKS**

Claims 22-30 and 32-58 are pending. Support for the amendment to Claim 42 is found throughout the specification; see for example, page 25, lines 8-11.

### **Rejections under 35 U.S.C. § 112, second paragraph**

Claims 42 and 46-50 are rejected under 35 U.S.C. § 112, second paragraph for being indefinite. Specifically, independent Claim 42 is rejected for lack of clarity because it does not identify a method. Claim 42 has been amended. Applicants respectfully request withdrawal of the rejection of Claims 42 and 46-50 under 35 U.S.C. § 112, second paragraph.

### **Rejection under 35 U.S.C. § 103(a)**

Claims 22-30 and 32-58 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lauffer et al (US 2002/0034476 A1) in view of Gries et al (U.S. Patent No. 5, 648, 063) in further view of Mathews and van Holde (1990, Biochemistry, pages 340-341).

As a preliminary matter, Applicants do not concede that Lauffer is prior art, or admit the propriety of the rejection. However, the rejection is moot because independent Claims 22, 30, 32, and 42 have a priority date based on U.S.S.N. 08/460,511 (i.e., '511 specification), which was filed on June 2, 1995. Support for the MRI agents disclosed in Claims 22, 30, 32, and 42 can be found throughout the '511 specification; for example see page 12, line 13 through page 14, line 11; page 23, lines 6-28; page 24, line 15 through page 26, line 5; and page 30, lines 4-27. Claims 23-29, 33-41, and 43-58 depend from and include all limitations of claims 22, 30, 32, and 42.

Assuming that the Lauffer reference is entitled to claim priority back to U.S.S.N. 60/014,448, the earliest possible priority date for the Lauffer reference is April 1, 1996. As

Claims 22-30 and 32-58 are entitled to a priority date of June 2, 1995, Applicants respectfully submit that Laufer is not 103 (a) art against Claims 22-30 and 32-58.

Gries discloses agents for use in NMR and X-ray diagnosis comprising complex salts and a paramagnetic ion to which biomolecules such as peptides and antibodies may be conjugated (see column 3, line 43 through column 4, line 7). Gries does not disclose MRI agents comprising a DOTA chelate, a paramagnetic ion, a linker, and a peptide blocking moiety.

Mathews and van Holde discloses six major classes of enzymes and their functions. Mathews and van Holde do not disclose MRI agents comprising a DOTA chelate, a paramagnetic ion, a linker, and a peptide blocking moiety.

The present invention, as disclosed in Claims 22-30 and 32-58, is directed to MRI agents comprising a DOTA chelator, a paramagnetic ion, a linker, and a peptide blocking moiety and methods of using these agents. Upon interaction of the peptide blocking moiety with a target substance, the peptide dislodges from the coordination site of the metal such that the  $T_1$  of the agent is decreased, thereby resulting in an enhanced MRI image. Thus, the MRI agents disclosed in Claims 22-30 and 32-58 are activatable, i.e., capable of being turned “on” and “off” through the interaction of the peptide moiety with its target substance.

To establish a *prima facie* case of obviousness the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991) M.P.E.P. §2143.

As argued above, Applicants respectfully submit that rejection based on Laufer in view of Gries and Mathews and van Holde does not apply against Claims 22-30 and 32-58; thus, the rejection under 103(a) based on Laufer et al (US 2002/0034476 A1) in view of Gries et al (U.S.

Patent No. 5, 648, 063) in further view of Mathews and van Holde (1990, Biochemistry, pages 340-341) should be withdrawn.

Moreover, there is no teaching in either Gries or Mathews and van Holde regarding an MRI agent comprising a component that is capable of turning on the agent via an interaction with a target substance such that the  $T_1$  of the agent is decreased. Therefore, the requirement of teaching or suggesting all the claim elements has not been met. Applicant respectfully submits the rejection under 35 U.S.C. § 103(a) does not apply to Claims 22-30 and 32-58.

Please direct any calls in connection with this application to the undersigned at (415) 781-1989.

Respectfully submitted,

DORSEY & WHITNEY LLP

By: 

Renee M. Kosslak, Reg. No 47,717  
for Robin M. Silva, Reg. No. 38,304  
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Four Embarcadero Center  
Suite 3400  
San Francisco, California 94111-4187  
Telephone: (415) 781-1989  
Fax No. (415) 398-3249